5.34 TIOTROPIUM
Capsule containing powder for oral inhalation 18 micrograms (as bromide monohydrate), Tiotropium Lupin™, Generic Health Pty Ltd.

1 Purpose of Submission

1.1 The Category 4 submission requested the listing of a new product containing tiotropium (as bromide monohydrate) 18 microgram powder for inhalation in capsules (Tiotropium Lupin™) for use with a new delivery device (LupinHaler®). The listing was requested for the treatment of chronic obstructive pulmonary disease (COPD) under the same circumstances as the currently listed tiotropium (as bromide monohydrate) 18 microgram powder for inhalation in capsules (Spiriva®) for use with a HandiHaler® device as an 'a'-flagged generic brand.

1.2 Listing was requested on the basis of a cost-minimisation approach versus Spiriva for use with a HandiHaler device.

2 Background

2.1 Spiriva (for use in HandiHaler) is currently listed on the PBS as a General Schedule Restricted Benefit listing for the treatment of COPD.

Registration status

2.2 Tiotropium Lupin was Therapeutic Goods Administration (TGA) registered on 28 August 2023 for the long-term maintenance treatment of bronchospasm and dyspnoea associated with COPD and the prevention of COPD exacerbations.

2.3 As part of its evaluation for registration, the TGA was satisfied that Tiotropium Lupin for use in LupinHaler could be considered bioequivalent to Spiriva for use in Handihaler.

Previous PBAC consideration

2.4 At its March 2019 meeting, in making its recommendation to list tiotropium 13 microgram powder for inhalation, Braltus®, as an alternative brand to Spiriva, the PBAC acknowledged concerns regarding the differences in labelled metered dose and delivery devices between Braltus and Spiriva. However, the PBAC considered that the differences in devices could be managed in the course of the regular patient education and counselling on the use of the devices that is provided to patients by prescribers and pharmacists, and that these differences were not sufficient to preclude marking

the two brands as equivalent (paragraph 5.7, tiotropium (Braltus), Public Summary Document, March 2019 PBAC Meeting).

2.5 Tiotropium Lupin has not been considered by the PBAC previously.

3 Requested listing

3.1 The submission requested the addition of a new product containing tiotropium (as bromide monohydrate) 18 microgram powder for inhalation under the same conditions as the existing listing for Spiriva.

Add new brand as follows:

<table>
<tr><th colspan="2">MEDICINAL PRODUCT
medicinal product pack</th><th>PBS item code</th><th>Max. qty packs</th><th>Max. qty units</th><th>№.of Rpts</th><th>Available brands</th></tr>
<tr><td colspan="7">TIOTROPIUM</td></tr>
<tr><td colspan="2">tiotropium 18 microgram powder for inhalation, 30 capsules</td><td>8626B
MP,NP</td><td>1</td><td>30</td><td>5</td><td>Spiriva
Tiotropium Lupin</td></tr>
<tr><td colspan="7"></td></tr>
<tr><td colspan="7">Restriction Summary 7839 / Treatment of Concept: 6352</td></tr>
<tr><td colspan="2" rowspan="3">Concept ID
(for internal Dept. use)</td><td colspan="5">Category / Program: GENERAL – General Schedule (Code GE)</td></tr>
<tr><td colspan="5">Prescriber type: ☒Nurse Practitioners ☒Medical Practitioners</td></tr>
<tr><td colspan="5">Restriction type: ☒Restricted benefit</td></tr>
<tr><td>Prescribing rule level</td><td></td><td colspan="5">Administrative Advice:
Pharmaceutical benefits that have the form tiotropium 18 microgram powder for inhalation and pharmaceutical benefits that have the form tiotropium 13 microgram powder for inhalation are equivalent for the purposes of substitution.</td></tr>
<tr><td colspan="2"></td><td colspan="5">Indication: Chronic obstructive pulmonary disease (COPD)</td></tr>
<tr><td colspan="2"></td><td colspan="5">Administrative Advice:
The treatment must not be used in combination with a LAMA/LABA or SAMA</td></tr>
<tr><td colspan="2"></td><td colspan="5">Administrative Advice:
A LAMA/LABA includes aclidinium/formoterol, glycopyrronium/indacaterol, tiotropium/olodaterol, or umeclidinium/vilanterol.</td></tr>
<tr><td colspan="2"></td><td colspan="5">Administrative Advice:
A SAMA includes ipratropium</td></tr>
<tr><td colspan="2"></td><td colspan="5">Administrative Advice:
Diagnosis of COPD should include measurement of airflow obstruction using spirometry, with confirmation of post-bronchodilator airflow obstruction.</td></tr>
<tr><td colspan="2"></td><td colspan="5">Administrative Advice:
Adherence to current treatment and device (inhaler) technique should be reviewed at each clinical visit and before "stepping up" a patient's medication regimen.</td></tr>
</table>

3.2 The submission requested that Tiotropium Lupin be marked as equivalent to Spiriva in the Schedule of Pharmaceutical Benefits for the purposes of substitution. The PBAC noted that Spiriva and Braltus are currently marked as equivalent for brand substitution ('a' flagging) by pharmacists at the point of dispensing.

3.3 The operational steps of the delivery devices for all three brands of tiotropium (Spiriva, Braltus and Tiotropium Lupin) are comparable. However, the Product Information (PI) for each brand states that each medicine is intended for use only with its respective

delivery device, and that there are differences in shelf-life (30 days for Zonda and LupinHaler; 1 year for HandiHaler).

3.4 As part of its December 2022 consideration, the PBAC recommended Spiriva and Braltus as suitable for listing on the PBS with increased maximum dispensed quantities (MDQ).

3.5 The guidance for exclusion of a medicine/medicine group from the increased MDQ for chronic conditions, which was accepted by the PBAC at its December 2022 meeting, states that 'Medicines must be PBS listed for 5 or more years, or generics of medicines which have been listed for 5 or more years, as severe but rare adverse effects frequently become evident during this period'.

3.6 Tiotropium (Spiriva) was listed on the PBS in February 2003. Braltus, the first generic brand for tiotropium, was PBS-listed in February 2020.

4 Consideration of the evidence

Sponsor hearing

4.1 There was no hearing for this item.

Consumer comments

4.2 The PBAC noted that no consumer comments were received for this item.

Pricing consideration

4.3 The submission requested the listing of Tiotropium Lupin on a cost-minimisation basis to Spiriva, as Tiotropium Lupin will directly substitute for the currently listed Spiriva if recommended for listing. The sponsor proposed an approved ex-manufacturer price (AEMP) for Tiotropium Lupin equivalent to that of Spiriva.

4.4 Braltus is marked as equivalent to Spiriva for the purposes of substitution at a lower AEMP. A comparison of the pack sizes and AEMPs for all three brands of tiotropium is outlined in Table 1.

Table 1: Price comparison across PBS-listed products as of February 2024

	Pack size	Price per pack (AEMP)
Sponsor Product		
Tiotropium Lupin	30 capsules	$28.82
Comparative Products		
Spiriva	30 capsules	$28.82
Braltus	30 capsules	$24.28

Source: ex-manufacturer prices (excluding Efficient Funding of Chemotherapy) - 1 February 2024
Abbreviations: AEMP = approved ex-manufacturer price

Estimated PBS usage and financial implications

4.5 The submission did not provide the estimated usage and financial implications of listing Tiotropium Lupin. However, given that the requested AEMP for Tiotropium Lupin was the same as that for Spiriva, it is expected that there would be no net

financial impact to the PBS/RPBS. This was based on the assumption that Tiotropium Lupin would substitute for Spiriva on a 1:1 basis without increasing the utilisation of tiotropium for the treatment of COPD.

4.6 As a Category 4 submission, the financial estimates have not been independently evaluated.

Quality Use of Medicines

4.7 Tiotropium Lupin is to be administered using a new device (LupinHaler), which is different from the delivery device for Spiriva (HandiHaler). While the operational procedures for the HandiHaler and LupinHaler are similar, there may be a need for adequate education for both patients and healthcare professionals on the use of the new device to ensure its correct and safe use.

4.8 Each pack of Tiotropium Lupin includes a patient information leaflet illustrating the proper administration of the LupinHaler device. The pre-PBAC response stated that with the appropriate education and counselling, any differences in the delivery devices could be managed. Furthermore, the pre-PBAC response noted that Quality Use of Medicines (QUM) resources, including instructional videos on usage and cleaning, along with an instructional PDF, will be available on the sponsor's website for Tiotropium Lupin, supplementing the usage instructions provided in the package leaflet.

5 PBAC Outcome

5.1 The PBAC recommended the General Schedule Restricted Benefit listing of a new product containing tiotropium, Tiotropium Lupin for use in LupinHaler, as an alternative to the currently PBS-listed reference brand, Spiriva for the treatment of chronic obstructive pulmonary disease (COPD). The PBAC's recommendation for listing was based on, among other matters, its assessment that the cost effectiveness for Tiotropium Lupin would be acceptable if it were cost-minimised to the lowest cost PBS-listed tiotropium brand for COPD.

5.2 The PBAC noted that the TGA concluded that bioequivalence has been established between Tiotropium Lupin (for use in LupinHaler) and Spiriva (for use in Handihaler).

5.3 The PBAC noted that Spiriva and Braltus (for use in Zonda device) are currently treated as equivalent (i.e., 'a' flagged) in the Schedule of Pharmaceutical Benefits. As such, the PBAC advised that, under Section 101(4AACD) of the *National Health Act 1953*, Tiotropium Lupin, Spiriva, and Braltus should be considered equivalent for the purposes of substitution (i.e., 'a' flagged in the Schedule with the following administrative advice: 'Pharmaceutical benefits that have the form tiotropium 18 microgram powder for inhalation and pharmaceutical benefits that have the form tiotropium 13 microgram powder for inhalation are equivalent for the purposes of substitution.').

5.4 The PBAC noted that while the operational steps of the delivery devices for all three brands of tiotropium (Spiriva, Braltus and Tiotropium Lupin) are very similar, each product is intended for use only with its respective delivery device, and these devices are not substitutable with each other at a patient level. However, the PBAC reiterated its previous consideration at its March 2019 meeting, where it advised that the differences in the delivery devices could be managed through regular patient education and counselling on the use of the devices, provided by prescribers and pharmacists. Furthermore, the PBAC expected that dispensing pharmacists would be responsible for communicating any change in device to patients and providing them with appropriate education on device administration. Consistent with this consideration, the PBAC was satisfied that sufficient education and QUM resources would mitigate any issues arising from the differences in the use of each device for tiotropium inhalation.

5.5 The PBAC noted that the sponsor planned to provide a range of QUM materials on its website for healthcare providers and patients.

5.6 The PBAC considered the listing of Tiotropium Lupin would not result in any additional cost to the PBS/RPBS as Tiotropium Lupin is expected to substitute for Spiriva or Braltus on a 1:1 basis.

5.7 The PBAC recommended Tiotropium Lupin as suitable for listing on the PBS with increased MDQ in line with its December 2022 consideration for Spiriva and Braltus.

5.8 The PBAC noted that its recommendation was on a cost-minimisation basis and advised that, because Tiotropium Lupin is not expected to provide a substantial and clinically relevant improvement in efficacy, or reduction of toxicity, over Spiriva or Braltus, or not expected to address a high and urgent unmet clinical need given the presence of an alternative therapy, the criteria prescribed by the *National Health (Pharmaceuticals and Vaccines – Cost Recovery) Regulations 2022* for Pricing Pathway A were not met.

5.9 The PBAC noted that this submission is not eligible for an Independent Review as it received a positive recommendation.

Outcome:
Recommended

6 Recommended listing

6.1 Add new medicinal product pack:

MEDICINAL PRODUCT medicinal product pack	**PBS item code**	**Max. qty packs**	**Max. qty units**	**№.of Rpts**	**Available brands**
TIOTROPIUM					
tiotropium 18 microgram powder for inhalation, 30 capsules	NEW *MP,NP*	1	30	5	*Tiotropium Lupin*

Restriction Summary 7839 / Treatment of Concept: 6352	
Concept ID (for internal Dept. use)	**Category / Program:** GENERAL – General Schedule (Code GE)
	Prescriber type: ☒Nurse Practitioners ☒Medical Practitioners
	Restriction type: ☒Restricted benefit
Prescribing rule level	**Administrative Advice:** Pharmaceutical benefits that have the form tiotropium 18 microgram powder for inhalation and pharmaceutical benefits that have the form tiotropium 13 microgram powder for inhalation are equivalent for the purposes of substitution.
	Indication: Chronic obstructive pulmonary disease (COPD)
	Administrative Advice: The treatment must not be used in combination with a LAMA/LABA or SAMA
	Administrative Advice: A LAMA/LABA includes aclidinium/formoterol, glycopyrronium/indacaterol, tiotropium/olodaterol, or umeclidinium/vilanterol.
	Administrative Advice: A SAMA includes ipratropium
	Administrative Advice: Diagnosis of COPD should include measurement of airflow obstruction using spirometry, with confirmation of post-bronchodilator airflow obstruction.
	Administrative Advice: Adherence to current treatment and device (inhaler) technique should be reviewed at each clinical visit and before "stepping up" a patient's medication regimen.

6.2 Add new item with increased MDQ:

MEDICINAL PRODUCT medicinal product pack	PBS item code	Max. qty packs	Max. qty units	№.of Rpts	Available brands
TIOTROPIUM					
tiotropium 18 microgram powder for inhalation, 30 capsules	*NEW* *MP,NP*	*2*	*60*	*5*	*Tiotropium Lupin*
Restriction Summary NEW / Treatment of Concept: NEW					
Concept ID (for internal Dept. use)	**Category / Program:** GENERAL – General Schedule (Code GE)				
	Prescriber type: ☒Nurse Practitioners ☒Medical Practitioners				
	Restriction type: ☒Restricted benefit				
Prescribing rule level	**Administrative Advice:** Pharmaceutical benefits that have the form tiotropium 18 microgram powder for inhalation and pharmaceutical benefits that have the form tiotropium 13 microgram powder for inhalation are equivalent for the purposes of substitution.				
	Indication: Chronic obstructive pulmonary disease (COPD)				
	Clinical criteria:				
	The condition must be stable for the prescriber to consider the listed maximum quantity of this medicine suitable for this patient.				
	Administrative Advice: The treatment must not be used in combination with a LAMA/LABA or SAMA				
	Administrative Advice: A LAMA/LABA includes aclidinium/formoterol, glycopyrronium/indacaterol, tiotropium/olodaterol, or umeclidinium/vilanterol.				
	Administrative Advice: A SAMA includes ipratropium				
	Administrative Advice: Diagnosis of COPD should include measurement of airflow obstruction using spirometry, with confirmation of post-bronchodilator airflow obstruction.				
	Administrative Advice: Adherence to current treatment and device (inhaler) technique should be reviewed at each clinical visit and before "stepping up" a patient's medication regimen.				

These restrictions may be subject to further review. Should there be any changes made to the restriction the sponsor will be informed.

7 Context for Decision

The PBAC helps decide whether and, if so, how medicines should be subsidised through the Pharmaceutical Benefits Scheme (PBS) in Australia. It considers applications regarding the listing of medicines on the PBS and provides advice about other matters relating to the operation of the PBS in this context. A PBAC decision in relation to PBS listings does not necessarily represent a final PBAC view about the merits of the medicine or the circumstances in which it should be made available through the PBS. The PBAC welcomes applications containing new information at any time.

8 Sponsor's Comment

Generic Health welcomes the PBAC recommendation for a General Schedule Restricted Benefit listing of Tiotropium Lupin, for use in LupinHaler, as an alternative to the currently PBS-listed reference brand, Spiriva for the treatment of chronic obstructive pulmonary disease (COPD).